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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
DAVIS,M	
ART UNIT	**PAPER NUMBER**
1642	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/331376	
Examiner	**Group Art Unit**
	1642

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 (MONTH(S)) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 08/14/00.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-4, 6-11, 13-16 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-4, 6-11, 13-16 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing R view, PTO-948

☐ Other _____

Office Acti n Summary

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claims 15-16.

Accordingly, claims 1-4, 6-11, 13-16 are being examined. It is noted that claim 12 has been canceled, and claims 1-4, 6-11, 13-14 have been amended.

The following are the remaining rejections.

OBJECTION

1. Claim 6 is objected to because claim 6 contains periods (.) which are not at the end of the claim.

2. Claim 6 is objected to because "drug resistance-related markers" and "melanoma-associated glycoprotein" are mispelled.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

1. Claims 1-4, 6-11, 13-16 are indefinite because it is not clear in claims 1 and 14 whether all or only some of the limitations following "optionally" are optional.

2. Claims 1-4, 6-11, 13-16 are indefinite because it is not clear in claims 1 and 14 whether particles coated with antibodies are used or whether only 2 to 6 antibodies are used.

3. Claims 1-4, 6-11, 13-16 are indefinite because claims 1 and 14 recite "0.5 particles. It is not clear what comprises 0.5 particles.

4. Claim 6 is indefinite because of the language "melanoma-associated glycoprotein", "pancreatic cancer associated marker", "colon cancer associated marker", "neuroblastoma associated epitope", "proliferation associated markers", "differentiation associated markers" "drug resistance related markers" "angiogenesis associated markers" and "invasion related antigens". It is not clear what kind of association or relation is referred to.

5. Claim 6 is indefinite because it is not clear what M. 160kD, and m.750 kD are. Does Applicant means MW? In addition, to be consistent, it is suggested that Applicant uses MW rather than Mw for molecular weight.

6. Claims 6, 8, 11, 13 are indefinite for the recitation of cancer antigens. Claim 1, from which claims 6, 8, 11, 13 directly or indirectly depend, specifically excludes malignant cell targets.

7. Claim 13 is indefinite because the language "the biologically informative markers" lacks antecedent, which is not found in claim 1 to which claim 13 is dependent. Furthermore, said language is indefinite, because it is not clear that the markers are informative for what.

8. Claim 13 is indefinite because it is not clear what a "par-human epitope' is.

9. For the clarity of the claims, it is suggested that in claims 1 and 14, the language "from 0.01um- 6um" is replaced with "from 0.01um to 6um", and the language "2-6" is replaced with "2 to 6".

REJECTION UNDER 35 USC 112, FOURTH PARAGRAPH, NEW REJECTION

Claim 7 is rejected under 35 USC 112, fourth paragraph, because it does not further limit the subject matter of the preceding claim.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Rejection under 35 USC 112, first paragraph of claims 1-4, 6-11, 13-14 pertaining to lack of enablement for a method to detect and phenotype any normal cells except malignant cells and nomal hematopoietic and lymphatic cells remains for reasons already of record in paper No. 10. New claims 15-16 are rejected under 35 USC 112, first paragraph, for the same reasons set forth for claims 1-4, 6-11, 13-14 in previous Office action.

Applicant argues that one would know to choose an antibody that would recognize a known antigen on a target cell of interest.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

The specification does not teach how to make antibodies or antigens specific for any normal cells that could distinguish one normal cell from others.

REJECTION UNDER 35 USC 102, NEW REJECTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 6-8, 11, 13, and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodstad et al (of record)..

Claims 1, 6-8, 11, 13, and 14-16 are drawn to a method and a kit to detect and phenotype target cells in cell suspensions, by using particles coated with antibodies directed against antigenic determinant/receptors expressed on target cells, except when the target cells are malignant and normal haematopoietic and lymphatic cells, wherein 2 to 6 antibodies are incubated under gentle rotation for about 5 minutes to about 2 hours with cell suspensions containing the target cells at 0^0C to 25^0C, optionally followed by an enrichment procedure, and evaluation of the target cell rosettes microscopically and/or by suitable visualizing or imaging devices, and wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01 um- 6 um, each antibody of the 2-6 antibodies is conjugated to different particles, and the ratio between the number of particles and the number of cells ranges from 0.5:1 to 20:1. The antibodies are directed against the

receptors/antigens as listed in claims 6, and 13, or against tumor associated antigens as listed in claim 8. The target cells are from an animal or a human.

Claims 1, 6-8, 11, 13, and 14-16 read on a method and a kit to detect and phenotype target cells in cell suspensions, by using particles coated with antibodies directed against antigenic determinant/receptors expressed on target cells, except when the target cells are malignant and normal haematopoietic and lymphatic cells, comprising 2 to 6 antibodies against any antigen, which are incubated under gentle rotation for about 5 minutes to about 2 hours with cell suspensions containing the target cells, at 0^0C to 25^0C. The following limitations are optional: 1) an enrichment procedure, 2) evaluation of the target cell rosettes microscopically and/or by suitable visualizing or imaging devices, and 3) one antibody conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01 um- 6 um, wherein each antibody of the 2-6 antibodies is conjugated to different particles, and the ratio between the number of particles and the number of cells ranges from 0.5:1 to 20:1. In other words, said 2-6 antibodies could be free, i.e. not conjugated to particles. Claims 1, 6-8, 11, 13, and 14 further read on either one of the following two possibilities: 1) the target cells are not malignant cells, and are not normal haematopoietic and lymphatic cells, or 2) the target cells could be malignant cells, provided said malignant cells are not haematopoietic and lymphatic cells.

Fodstad et al teach a method and a kit for detecting specific target cells in cell suspensions, by mixing target-cells-associating antibodies, which are attached to particles, or free

target-cells-associating antibodies, with the cell suspension for 5-10 min to 2 h, at a temperature between 0^0C and 20^0C, under gentle rotation (claims 1, 1.2.1, 1.2.2 and 16). Fodstad et al teach that the cell suspension is incubated with a second set of antibodies which are prelabeled or not with fluorescent agents (abstract). In other words, at least two antibodies are incubated with target cells under the above mentioned condition. Fodstad et al teach that the targeted antigens could be antigens in normal, living cells, i.e. liver hepatocytes, endothelial cells, and that the antigens are EGF-receptor, integrins, or other adhesion membrane molecules in normal cells (claims 2, 4, 5, and table 1), or tumor antigens from a patient (claim 10 and table 1) .

Thus the method and the kit taught by Fodstad et al are the same as the claimed invention, meeting all the limitations of the claimed invention.

REJECTION UNDER 35 USC 103

Rejection under 35 USC 103 of claims 1-4, 6-11, 13-14 pertaining to obviousness over Kajek et al, in view of Fostad et al, and O'Briant et al remains for reasons already of record in paper No. 10. New claims 15-16 are rejected under 35 USC 103 for the same reasons set forth for claims 1-4, 6-11, 13-14 in previous Office action.

Applicant argues as follows:

Hajek uses a cell population comprising many cells, i.e. bone marrow cells which are coarsely sorted out from large cell population. The method of Hajek et al is a screening method not requiring high specificity and sensitivity.

Like Hajek, the method of O'Briant lacks the specificity required by the presently claimed invention.

In addition, one would not have using the teaching of Fodstad in arriving at the present invention because the conditions for using paramagnetic beads of Fodstad are different from the conditions for using non-paramagnetic beads, i.e. the former contains iron and are also much heavier.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

Besides bone marrow cells, Hajek et al also teach that the disclosed method could be applied to cancer cells. Thus the method of Hajek et al comprises the same types of microspheres, bound to antigen specific antibodies, and optically characterized for sorting by size, shape, and color as the claimed method. Furthermore, in combination with the method of Fostad et al for optimal conditions of incubation, optimal ratio of particles and tumor cells, and relevant tumor antigens, the combined methods of Hajek et al and Fostad et al seem to be the same as the claimed method, using the same reagents and conditions. Thus one of ordinary skill in the art would have expected that the combined methods of Hajek et al and Fostad et al would provide the same specificity and sensitivity as the claimed method.

Thus, the claimed method appears to be the same as the prior art combined method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the combined method of the prior

art does not possess the same specificity and sensitivity of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

In addition, although Fostad et al use paramagnetic beads, the conditions taught by Fostad et al, such as duration of incubation, temperature, and the ratio of particles and tumor cells are for optimal binding between antibodies on the beads and antigens on tumor cells, and thus could be applied as well for non-paramagnetic beads, wherein the presence of iron in the paramagnetic beads would not affect the binding between antibodies on the beads and antigens on tumor cells. Furthermore, with regards to the incubation conditions and the ratio of particles and tumor cells, as recited in the claims, to determine optimum incubation conditions and ratio of particles and tumor cells is within the level of ordinary skill in the art. See In re Kronig, 190 USPQ 425.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

October 28, 2000

SUSAN UNGAR, PH.D
PRIMARY EXAMINER